AMENDMENTS TO THE CLAIMS

1. (Currently amended) A targeting vector comprising:
   a) a first sequence homologous to a portion or region of a target gene;
   b) a second sequence homologous to a portion or region of a target gene;
   c) a selectable marker cassette located between the first sequence and second sequence; and
   d) a regulator, wherein the regulator is located outside the first sequence and second sequence and controls expression of the selectable marker;

   wherein the targeting vector is capable of modifying the target gene.
2. (Original) The targeting vector of claim 1, wherein the selectable marker cassette comprises a promoter region and a sequence encoding a selectable marker.
3. (Original) The targeting vector of claim 2, wherein the selectable marker is a marker conferring antibiotic resistance.
4. (Original) The targeting vector of claim 3, wherein the selectable marker conferring antibiotic resistance is a neomycin resistance gene.
5. (Original) The targeting vector of claim 2, wherein the promoter region comprises a promoter sequence.
6. (Original) The targeting vector of claim 5, wherein the promoter sequence is a PGK promoter sequence.
7. (Original) The targeting vector of claim 6, wherein the promoter region further comprises at least one operator sequence.
8. (Currently amended) The targeting vector of claim 7~~6~~, wherein the operator sequence is a lac operator sequence.
9. (Original) The targeting vector of claim 6, wherein the promoter region comprises the sequence set forth in SEQ ID NO:2.
10. (Original) The targeting vector of claim 1, wherein the regulator inhibits expression of the selectable marker.
11. (Canceled)
12. (Original) The targeting vector of claim 1, wherein the regulator comprises at least one repressor sequence.
13. (Original) The targeting vector of claim 12, wherein the repressor sequence is a lac repressor sequence.

14. (Original) The targeting vector of claim 13, wherein the regulator further comprises a nuclear localization signal.

15. (Original) The targeting vector of claim 14, wherein the regulator comprises the sequence set forth in SEQ ID NO:3.

16. (Original) The targeting vector of claim 1, wherein the regulator comprises a transcriptional silencer element.

17. (Original) The targeting vector of claim 14, wherein the nuclear localization sequence is positioned upstream of the repressor sequence.

18. (Currently amended) A method of producing cells comprising a modification of a target gene, the method comprising:

a) introducing into cells capable of homologous recombination a targeting vector, wherein the targeting vector comprises:

i) a first sequence homologous to a portion or region of the target gene;

ii) a second sequence homologous to a portion or region of the target gene;

iii) a selectable marker cassette located between the first sequence and second sequence; and

iv) a regulator, wherein the regulator is located outside the first sequence and second sequence and controls expression of the selectable marker;

b) selecting for cells expressing the selectable marker; and

c) identifying cells containing the modification of the target gene.

19. (Original) The method of claim 18, wherein the cells are embryonic stem cells.

20. (Currently amended) A method of identifying cells comprising a disruption or modification of a target gene, the method comprising:

a) introducing into cells capable of homologous recombination a targeting vector, wherein the targeting vector comprises:

i) a first sequence ~~substantially~~ homologous to a portion or region of the target gene;

ii) a second sequence ~~substantially~~ homologous to a portion or region of the target gene;

iii) a selectable marker cassette located between the first sequence and second sequence; and

iv) a regulator located outside the first sequence and second sequence, wherein the regulator is capable of controlling expression of a selectable marker, wherein the

selectable marker is positioned within the selectable marker cassette; and wherein the targeting vector is capable of modifying the target gene;

b) selecting for cells expressing the selectable marker; and

c) identifying cells comprising the disruption or modification of the target gene.

21. (Currently amended) The method of claim 20~~22~~, wherein the cells are embryonic stem cells.

22. (Currently amended) A method of enriching for cells comprising a disruption or modification of a target gene, the method comprising:

a) inserting into cells capble of homologous recombination a targeting vector comprising:

i) a first sequence ~~substantially~~ homologous to a portion or region of the target gene;

ii) a second sequence ~~substantially~~ homologous to a portion or region of the target gene;

iii) a selectable marker cassette located between the first sequence and second sequence; and

iv) a regulator located outside the first sequence and second sequence, wherein the regulator is capable of controlling expression of a selectable marker, wherein the selectable marker is positioned within the selectable marker cassette; and wherein the targeting vector is capable of modifying the target gene;

b) selecting for cells in which the targeting vector has integrated into the genomes of the cells via homologous recombination, wherein the selected cells express the selectable marker; and

c) identifying cells containing the disruption or modification of the target gene.

23. (Currently amended) The method of claim 22~~24~~, wherein the method enhances recovery of cells having the targeting vector integrated via homologous recombination into the genomes of the cells.

24. (Currently amended) The method of claim 22~~24~~, wherein the cells are embryonic stem cells.

25. (Currently amended) The method of claim 22~~24~~, wherein the targeting vector is introduced in the cells by electroporation.

26. (Currently amended) An isolated host cell comprising a modification or disruption of a target gene, wherein the target gene is modified or disrupted by insertion of ~~a~~ the targeting vector of claim 1 into the host cell.

27. (Withdrawn) A method of producing a transgenic animal having a genome comprising a modification or disruption of a target gene, the method comprising:

a) introducing a targeting vector into a cell;

b) selecting cells expressing the selectable marker and identifying the cells containing the modification or disruption of the target gene;

c) inserting the cells identified in step (b) into an embryo ; and

d) propogating the transgenic animal from the embryo.

28. (Withdrawn) A transgenic animal comprising a modification or disruption of a target gene within the genome of the transgenic animal, wherein the modification or disruption of the target gene is produced by:

a) introducing a targeting vector into a cell;

b) selecting cells expressing the selectable marker and identifying the cells containing the modification or disruption of the target gene;

c) inserting the cells identified in step (b) into an embryo ; and

d) propogating the transgenic animal from the embryo.

29. (Currently amended) A method of modifying or disrupting the function of a target DNA sequence, the method comprising introducing a targeting vector into a cell, thereby producing a homologous recombinant, wherein the function of the target gene is modified or disrupted, and wherein the targeting vector comprises:

a) a first sequence homologous to a portion or region of the target DNA sequence;

b) a second sequence homologous to a portion or region the target DNA sequence;

c) a selectable marker cassette located between the first sequence and second sequence; and

d) a regulator located outside the first sequence and second sequence, wherein the regulator is capable of controlling expression of a selectable marker,

wherein the selectable marker is positioned within the selectable marker cassette.

30. (Currently amended) A method of producing a ~~an~~ targeting vector, the method comprising:

a) generating a first sequence homologous to a portion or region of a target DNA sequence;

b) generating a second sequence homologous to a portion or region of a target DNA sequence;

c) generating a selection marker cassette;

d) generating a regulator, wherein the regulator controls expression of a selectable marker;

e) and cloning a, b, c, and d into a vector to produce a targeting vector such that the selection marker cassette is located between the first sequence and second sequence and

the regulator is located outside the first sequence and second sequence.

31. (Currently amended) The method of claim 3013, wherein the targeting vector comprises SEQ ID NO:13.